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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,208	10/12/2001	Leendert Koenderman	7238/0J504	9804

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Bert J. Lewen
Darby & Darby
805 Third Avenue
New York, NY 10022-7513

EXAMINER

BELYAVSKIY, MICHAEL A

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 05/06/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N .

09/869,208

Applicant(s)

KOENDERMAN ET AL.

Examiner

Michail A Belyavskyi

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10/12/01 and 13 February 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) 1 and 5-13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-4 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 October 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3. 6) ☐ Other: _____

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DETAILED ACTION

1. Claims 1-13 are pending.

2. Applicant's election with traverse of Group II, Claims 2-4, Paper NO:9 is acknowledged. Applicant's traversal is on the grounds that the entire restriction requirement be reconsidered because the present application is a national phase application under 37 C.F.R. § 371 and no unity of invention issue was raised during prosecution of original claims in the PCT application by either the International Search Authority or the International Preliminary Examination Authority. This is not found persuasive because : (i) Applicants are reminded that the findings and opinion of the PCT examining authority is not controlling authority for the USPTO; (ii) CFR 1.475 (a) indicates that a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. CFR 1.475(e) indicates that the determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim (MPEP R-90 -- R-91 and 1893.03(d)). The restriction requirement complied with 37 CFR 1.475 in setting Groups I-III for reasons elaborated in paragraphs 2-3 of the previous Office Action , Paper No. 7, mailed 12/16/02

The requirement is still deemed proper and is therefore made FINAL.

Claims 1 and 5-13 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 2-4 are under consideration in the instant application.

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3. Formal drawings have been submitted which fail to comply with 37 CFR 1.84. Please see the enclosed form PTO-948.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in ABANDONMENT of the application.

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4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 2-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

6. In claims 2-4 it is apparent that bacteriophage isolated from strains A17 and A27 having accession numbers CBS 101481 and 101482 accordingly are required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of said strains. See 37 CFR 1.801-1.809.

It is noted that the specification on page 7, lines 30-35, indicates strains have been deposited with the CBS.

If the deposit have been made under the terms of the Budapest treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the strains A17 and A27 have been deposited under the Budapest Treaty and that the strains A17 and A27 will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample or for the enforceable life of the patent whichever is longer. See 37 CFR 1.806.

If the deposit has not been made under the Budapest treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in position to make such assurances, or statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

Also an issue is that the specification does not reasonably provide enablement for *any* phagocyte-recognizing agent wherein *any* phagocyte-recognizing agent recognizes the agent that is recognized by at least one bacteriophage as can be isolated from the strain having accession number CBS 101481 and 101482 (clone A17 and A27 respectively). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

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The specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation.

The claims as written encompass the genus of “phagocyte-recognizing agent” that can specifically recognize the “agent” that is recognized by at least one bacteriophage isolated from strains A17 and A27 wherein said recognized “agent” not even disclosed.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

There is insufficient guidance and direction as to how to make *any* phagocyte-recognizing agent wherein *any* phagocyte-recognizing agent recognizes the agent that is recognized by at least one bacteriophage isolated from strains A17 and A27. Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies such “phagocyte-recognizing agent” other than specific bacteriophage isolated from strains A17 and A27 having accession number CBS 101481 and 101482. While “*any* phagocyte-recognizing agent” may have some notion of the activity of bacteriophage isolated from strains A17 and A27, claiming biochemical molecules by such properties fails to provide sufficient guidance and direction as to how the skilled artisan can make and use such “phagocyte-recognizing agent”, commensurate in scope with the claimed invention. It has been well known to those skilled in the art at the time the invention was made that minor structural differences among structurally related compounds or compositions can result in substantially different pharmacological activities. Applicant has not enabled structurally related and unrelated compounds comprising *any* phagocyte-recognizing agent recognizes the agent that is recognized by at least one bacteriophage isolated from strains A17 and A27 would be expected to have greater differences in their activities. There is insufficient direction or objective evidence as to how to make and to how to use any agent which recognizes the agent that is recognized by at least one bacteriophage isolated from strains A17 and A27 (e.g. desired/intended effect of the claimed limitations). Moreover, the present specification failed to provide any biochemical and structural characteristics of the ‘agent’, or “epitope” that is recognized by specific bacteriophage isolated from strains A17 and A27 having accession number CBS 101481 and 101482. The common attributes of such “agent” or ‘epitope’ are not described.

Colman *et al.*, in *Research in Immunology* (145(1):33-36, 1994) teach single amino acid changes in an antigen can effectively abolish antibody antigen binding. Abaza *et al.*, in *Journal of Protein Chemistry* (11(5):433-444, 1992) teach that single amino acid substitutions outside the antigenic site on a protein effect antibody binding. Further, Lederman *et al* in *Molecular Immunology* (28:1171-1181, 1991) disclose that a single

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amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document).

The current state of the art in epitope structure prediction is limited given the noncontiguous amino acid residues constitute most epitopes, and that the dynamics of binding is often not integrated into the epitope prediction equation, making epitope structure prediction a complex four-dimensional problem (see Van Regenmortel, page 464, abstract in particular; Methods: A Companion to Methods of Enzymology 9:465-472, 1996). Van Regenmortel notes that 90% of antibodies raised against intact proteins do not react with any peptide fragment derived from the parent protein indicating that these antibodies are directed to discontinuous epitopes (see page 466, column 1 in particular). In addition Van Regenmortel states that the low success rate of antigenic prediction is due to the fact that predictions concern only continuous epitopes and it is unrealistic to reduce the complexity of epitopes that always possess conformational features to one-dimensional, linear peptide models (see page 467, column 2 in particular). Detailed information regarding the specific epitopes recognized by the instant specific bacteriophage isolated from strains A17 and A27 having accession number CBS 101481 and 101482 is lacking. Therefore, predicting which “phagocyte-recognizing agent” outside of “bacteriophage isolated from strains A17 and A27 having accession number CBS 101481 and 101482” is well outside the realm of routine experimentation. A skilled artisan would require guidance, such as the structure and biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) of the agent recognized by bacteriophage isolated from strains A17 and A27 successfully used in the instant invention in order to provide enablement for *any* phagocyte-recognizing agent wherein *any* phagocyte-recognizing agent recognizes the agent that is recognized by at least one bacteriophage as can be isolated from the strain having accession number CBS 101481 and 101482 in a manner reasonably commensurate with the scope of the claims. Thus, it would require undue experimentation of one skilled in the art to practice the claimed invention.

Because of this lack of guidance, an undue experimentation would be required to determine which modifications would be acceptable to retain occluding structural and functional activity, and the fact that the relationship between the sequence of a protein/peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g. see Ngo *et al* in the Protein Folding problem and Tertiary Structure prediction, 1994, Merz *et al.*, (ed), Birkhauser, Boston, MA, pp.433 and 492-495), it would require an undue amount of experimentation for one of skill in the art to arrive at the claimed *any* phagocyte-recognizing agent wherein *any* phagocyte-recognizing agent recognizes the agent that is recognized by at least one bacteriophage as can be isolated from the strain having accession number CBS 101481 and 101482 encompassed by the claimed invention.

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The scope of the claimed *any* phagocyte-recognizing agent wherein *any* phagocyte-recognizing agent recognizes the agent that is recognized by at least one bacteriophage as can be isolated from the starain having accession number CBS 101481 and 101482 is not commensurate with the enablement provided by the disclosure of specific bacteriophage isolated from the starain having accession number CBS 101481 and 101482. with regard to the extremely large number of amino acid sequences broadly encompassed by the claimed invention. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's or peptide's amino acid sequence, and, in turn, nucleic acid sequence and still retain similar biological activity or structural specificity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a limited number of proteins and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed *any* phagocyte-recognizing agent recognizes the agent that is recognized by at least one bacteriophage as can be isolated from the starain having accession number CBS 101481 and 101482 in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

7. Claims 2-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of : phagocyte-recognizing agent , wherein phagocyte-recognizing agent is a bacteriophage clones isolated from strains A17 and A24 with accession numbers CBS 101481 and 101482.

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Applicant is not in possession of : *any* phagocyte-recognizing agent recognizes the agent that is recognized by at least one bacteriophage as can be isolated from the strain having accession number CBS 101481 and 101482.

Applicant has disclosed a limited number of species; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

A description of a genus of phagocyte-recognizing agent may be achieved by means of a recitation of a representative number of agents, defined by amino acid sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly & Co., 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 “Written Description” Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

8. No claim is allowed.

9. The prior art does not teach or suggest the claimed invention recited in claims 2-4.

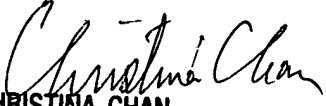
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10. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. For example, on page 1, line 18 the term "biopt" and on page 1, line 27 the phrase ' the thus' are misspelled. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
March 5, 2003


CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600